



## Original article

# Comparison of clinical outcomes between octogenarians and non-octogenarians with acute myocardial infarction in the drug-eluting stent era: Analysis of the Korean Acute Myocardial Infarction Registry



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## ARTICLE INFO

## Article history:

Received 30 April 2012

Received in revised form

18 November 2012

Accepted 13 April 2013

Available online 31 May 2013

## Keywords:

Elderly

Myocardial infarction

Treatment

Prognosis

## ABSTRACT

**Background and purpose:** Octogenarians (age  $\geq 80$  years) with coronary artery disease constitute a high-risk group. However, octogenarian patients with acute myocardial infarction (AMI) in the drug-eluting stents (DES) era have not been widely reported. We aimed to identify clinical outcomes in octogenarian compared with non-octogenarian AMI patients.

**Methods and subjects:** We retrospectively analyzed 9877 patients who underwent percutaneous coronary intervention (PCI) with drug-eluting stents (DES) and who were enrolled in the Korean Acute Myocardial Infarction Registry (KAMIR). They were divided into 2 groups, octogenarians ( $n = 1494$ ) and non-octogenarians ( $n = 8383$ ), in order to compare the incidence of 1-year all-cause death and 1-year major adverse cardiac events (MACE), where MACE included all-cause death, recurrent myocardial infarction, target vessel revascularization (TVR), target lesion revascularization (TLR), and coronary artery bypass grafting (CABG).

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**Results:** The clinical status was significantly inferior in octogenarians compared to non-octogenarians: Killip class  $\geq$  II (34.8% vs. 22.5%,  $p < 0.001$ ), multivessel disease (65.8% vs. 53.7%,  $p < 0.001$ ). Rates of 1-year all-cause death were significantly higher in octogenarians than in non-octogenarians (22.3% vs. 6.5%,  $p < 0.001$ ). However, the rates of 1-year recurrent myocardial infarction (1.3% vs. 0.9%,  $p = 0.68$ ), TLR (2.4% vs. 3.1%,  $p = 0.69$ ), TVR (3.6% vs. 4.3%,  $p = 0.96$ ), and CABG (0.9% vs. 0.9%,  $p = 0.76$ ) did not differ significantly between the 2 groups.

**Conclusions:** Octogenarian AMI patients have higher rates of mortality and MACE even in the DES era. According to KAMIR subgroup analysis, the TLR/TVR rates in octogenarians were comparable to those in non-octogenarian AMI patients.

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## Introduction

Percutaneous coronary intervention (PCI) has become the primary treatment for acute myocardial infarction (AMI) [1]. Furthermore, PCI with drug-eluting stents (DES) has been reported to markedly reduce the incidence of restenosis and target lesion revascularization (TLR) [2–5].

The octogenarian population (age  $\geq$  80 years) is rapidly growing and these patients are often at the highest risk of procedural complications during PCI, owing to their greater prevalence of associated comorbidities and more depressed cardiac function [6–9]. However, there are only limited data regarding octogenarian AMI patients who undergo PCI in the current DES era, because octogenarians are less commonly enrolled in randomized clinical trials, while observational studies include only a relatively small number of patients. The aim of this study was to identify the clinical outcomes in octogenarian AMI patients who underwent PCI with DES, compared with non-octogenarian AMI patients (age  $<$  80 years).

## Methods

### Study population

This study was based on a database collected by the Korean Acute Myocardial Infarction Registry (KAMIR) National Registry Study. KAMIR is a prospective, multicenter registry that was designed to characterize the clinical features and 1-year prognosis of AMI in Korean patients. All 51 community and teaching hospitals in Korea were invited to participate in KAMIR. A total of 14,885 patients with suspected AMI at admission were enrolled in KAMIR from January 2006 to December 2008.

A total of 9877 consecutive patients who underwent PCI with DES and whose discharge diagnosis was AMI were included in the present study. The patients were divided into 2 groups: octogenarians ( $n = 1494$ , mean age  $\pm$  1SD =  $84 \pm 4$  years, range 80–99 years) and non-octogenarians ( $n = 8383$ , age  $63 \pm 11$  years, range 30–79 years). An age of 80 years was determined to be an appropriate cut-off point, based on a recent report that the event rate is significantly higher in patients aged  $\geq$  80 years compared to those aged  $<$  80 years [10].

This analysis compared the following data and endpoints between the 2 groups: (1) baseline clinical and angiographic findings; (2) 1-year all-cause death; and (3) 1-year major adverse cardiac events (MACE), including all-cause death, recurrent myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), and coronary artery bypass grafting (CABG).

### Study protocol and data collection and management

Patients were enrolled in KAMIR after being admitted to participating hospitals with a suspected diagnosis of AMI. Detailed data were collected at each institution by a study coordinator or doctor, who entered the data into a password-protected, web-based,

computerized database provided by the KAMIR committee. Data coordinators attended meetings at least twice yearly. In addition, they reviewed and discussed the study protocol.

At participating sites, consecutive patients admitted with AMI were asked to register for the study. All treatment strategies, including reperfusion therapy modality and medications, were chosen at the discretion of the attending physicians. This study protocol was reviewed and approved by the institutional review boards of the participating centers.

### Medical treatment and PCI procedure

All patients received a 300-mg loading dose of aspirin and a 300–600-mg loading dose of clopidogrel and heparin prior to the procedure. During the procedure, weight-adjusted unfractionated heparin was administered in a bolus dose of 100 U/kg, with an additional bolus to maintain an activated clotting time of 250–300 s. Following the PCI/DES procedure, 100–300 mg/day of aspirin was continued indefinitely, and 75 mg/day of clopidogrel was continued for  $\geq$  12 months according to guidelines [11,12]. The choice of the specific type of DES was left to the operator's discretion. Coronary perfusion pre- and post-PCI was evaluated according to the Thrombolysis in Myocardial Infarction (TIMI) perfusion grading system. Clinical follow up was performed at 1, 6, and 12 months, and when angina-like symptoms occurred.

### Definitions and clinical endpoints

AMI was diagnosed according to the European Society of Cardiology/American College of Cardiology diagnostic criteria [13]. AMI was diagnosed by characteristic clinical presentation, serial changes on the electrocardiogram suggesting myocardial infarction, and elevated cardiac enzymes. ST-segment elevation MI was defined as new ST elevation in  $\geq$  2 contiguous leads. A history of hypertension was defined as systolic blood pressure  $\geq$  140 mmHg and/or diastolic blood pressure  $>$  90 mmHg at rest on admission, or treatment with anti-hypertensive medications. Diabetes mellitus was defined as the use of an oral hypoglycemic agent or insulin to lower blood glucose levels. Hyperlipidemia was defined as a total cholesterol level  $>$  200 mg/dl or treatment with a lipid-lowering agent. Coronary artery disease was defined as a history of MI, revascularization procedure, or obstructive coronary artery disease. Echocardiography was performed in all patients; left ventricular ejection fraction was assessed using the modified Simpson's biplane method. Recurrent MI was defined as the recurrence of symptoms or the presence of electrocardiographic changes in association with a rise in cardiac biomarker levels above the upper limit of normal. Death was considered to be cardiac-related unless non-cardiac death could be defined clearly. The primary endpoint of this study was the incidence of all-cause death, including in-hospital death, at 1 year of follow up. The secondary endpoint was the 1-year incidence of MACE. The predictors of all-cause death and MACE at 1 year of follow up were also investigated.

## Statistical analysis

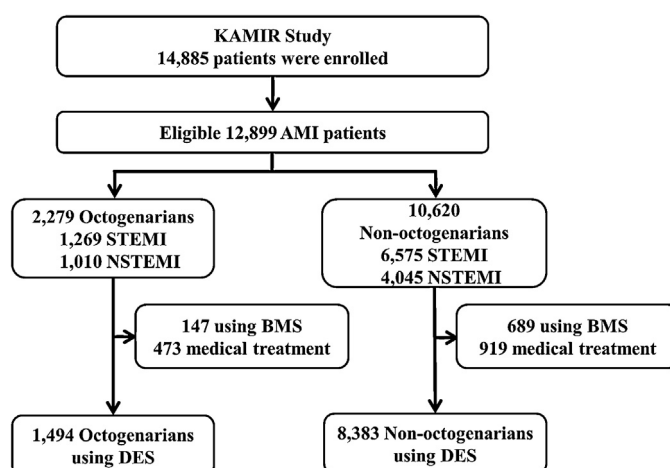
All eligible patients enrolled in this registry were included in the analysis. SPSS 18.0 for Windows software (SPSS Inc., Chicago, IL, USA) was used for all analyses. Continuous variables were presented as mean  $\pm$  standard deviation and were compared using Student's *t*-test or the Mann–Whitney *U*-test. Discrete variables are presented as counts and percentages, and were compared using chi-square statistics or Fisher's exact test, as appropriate. Standard statistics were used to describe the baseline clinical and lesion characteristics, and the procedural and clinical outcomes. Cox regression analysis was performed to identify independent predictors of 1-year mortality and MACE between octogenarian and non-octogenarian patients. Variables with  $p < 0.2$  in univariate were included in Cox models.

## Results

### Patients, lesions, and procedural characteristics

The flow chart in Fig. 1 shows the enrolment protocol, which resulted in the 2 study groups: octogenarians ( $n = 1494$ , mean age  $\pm$  1SD =  $84 \pm 4$  years, range 80–90 years) and non-octogenarians ( $n = 8383$ , age  $63 \pm 11$  years, range 30–79 years).

The baseline characteristics of the 2 groups are shown in Table 1. Significant differences were observed between the 2 groups. Patients in the octogenarian group were more likely to have atypical chest pain or painless MI and were also more likely to have renal dysfunction (estimated glomerular filtration rate,  $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ ) and a history of cerebral vascular accident. The proportion of men was higher in the non-octogenarian group. The prevalence of hypertension was significantly higher, whereas the prevalence of hyperlipidemia, current smoking, and family history of coronary artery disease were significantly lower in octogenarians than in non-octogenarians. The clinical condition was also significantly inferior in octogenarians, with lower blood pressure, lower left ventricular ejection fraction, more frequent Killip class  $\geq \text{II}$  (34.8% vs. 22.5%,  $p < 0.001$ ), higher high-sensitivity



**Fig. 1.** Flowchart illustrating the enrolment of patients in the study. KAMIR, Korean Acute Myocardial Infarction Registry; AMI, acute myocardial infarction; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; BMS, bare metal stent; DES, drug-eluting stents.

C-reactive protein (hs-CRP) level ( $p < 0.001$ ), and higher N-terminal pro-B-type natriuretic peptide (NT-proBNP) level ( $p < 0.001$ ). The rate of ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) was not significantly different between the groups.

The baseline coronary angiographic observations and procedural outcomes in each group are shown in Table 2. There were no significant differences in the types of culprit lesion between the 2 groups. The octogenarian group exhibited significantly more multivessel disease (65.8% vs. 53.7%,  $p < 0.001$ ), higher rates of post-PCI TIMI flow grade 0 or 1 flow (3.8% vs. 2.4%,  $p = 0.01$ ), and a lower rate of post-PCI TIMI flow grade 3. In the hospital and at discharge, octogenarians were less likely to receive evidence-based medical treatment, including glycoprotein IIb/IIIa inhibitor, aspirin, clopidogrel,  $\beta$ -blocker, or statin ( $p < 0.001$ ).

**Table 1**  
Patient characteristics of octogenarians and non-octogenarians.

	Octogenarians ( $n = 1494$ )	Non-octogenarians ( $n = 8383$ )	<i>p</i> -Value
Age (years)	$84 \pm 4$	$63 \pm 11$	$< 0.001$
Male, $n$ (%)	681 (45.6)	6438 (76.9)	$< 0.001$
BMI ( $\text{kg/m}^2$ )	$24 \pm 3.2$	$24 \pm 3.1$	0.436
History, $n$ (%)			
Hypertension	847 (56.7)	3880 (46.3)	$< 0.001$
Dyslipidemia	71 (4.8)	859 (10.2)	$< 0.001$
Diabetes mellitus	395 (26.4)	2290 (27.3)	0.482
Smoking	550 (36.8)	5246 (62.6)	$< 0.001$
Family history of CAD	39 (3.0)	613 (8.2)	$< 0.001$
Previous coronary interventions	66 (4.4)	446 (5.3)	0.147
Old myocardial infarction	59 (3.9)	273 (3.3)	0.171
Peripheral vascular disease	24 (3.7)	63 (2.0)	0.011
Cerebral vascular accident	142 (21.7)	463 (14.9)	$< 0.001$
Estimated GFR $< 60$ ( $\text{ml/min/1.73 m}^2$ ), $n$ (%)	674 (45.8)	1879 (22.9)	$< 0.001$
Initial presentation			
Atypical symptom, $n$ (%)	274 (18.5)	1049 (12.6)	$< 0.001$
Painless myocardial infarction, $n$ (%)	261 (17.6)	1009 (12.1)	$< 0.001$
Heart rate (beats/min)	$77 \pm 22$	$77 \pm 28$	0.39
Systolic blood pressure (mmHg)	$125 \pm 30$	$129 \pm 33$	$< 0.001$
Diastolic blood pressure (mmHg)	$75 \pm 17$	$79 \pm 26$	$< 0.001$
Killip class ( $\geq \text{II}$ ), $n$ (%)	502 (34.8)	1824 (22.5)	$< 0.001$
Peak troponin I (ng/ml)	$49 \pm 166$	$50 \pm 145$	0.912
hs-CRP (mg/dl)	$18 \pm 66$	$12 \pm 51$	$< 0.001$
NT-proBNP (pg/ml)	$4682 \pm 7846$	$1700 \pm 4777$	$< 0.001$
LVEF $< 40\%$ , $n$ (%)	260 (19.8)	1006 (13.3)	$< 0.001$

Data are presented as the  $n$  (%) of patients or mean  $\pm$  SD. BMI, body mass index; CAD, coronary artery disease; GFR, glomerular filtration rate; hs-CRP, high-sensitivity C-reactive protein; NT-pro-BNP, N-terminal pro-B type natriuretic peptide; LVEF, left ventricular ejection fraction.

**Table 2**  
Characteristics of procedures and medical treatment during hospitalization.

	Octogenarians (n = 1494)	Non-octogenarians (n = 8383)	p-Value
<b>Procedures</b>			
STEMI, n (%)	953 (63.8)	5481 (65.4)	0.234
Primary PCI	797 (84.9)	4345 (80.1)	0.001
Facilitated PCI	22 (2.3)	189 (3.5)	0.071
NSTEMI, n (%)	541 (36.2)	2902 (34.6)	0.234
Multivessel PCI, n (%)	348 (24.6)	1842 (23.4)	0.317
Complete revascularization, n (%)	162 (11.4)	1025 (13.0)	0.107
Culprit coronary artery, n (%)			
Left main	2 (0.1)	37 (0.5)	0.081
Left anterior descending	681 (45.9)	3947 (48.5)	0.173
Left circumflex	214 (14.6)	1372 (16.7)	0.045
Right coronary artery	543 (37.1)	2696 (32.9)	0.002
ACC/AHA type B2/C, n (%)	1072 (79.2)	5834 (77.0)	0.079
Number of diseased vessels, n (%)			
One-vessel disease	477 (32.6)	3657 (44.5)	<0.001
Two-vessel disease	488 (33.3)	2558 (31.2)	0.099
Three-vessel disease	462 (31.6)	1805 (22.0)	<0.001
Multi-vessel disease	964 (65.8)	4406 (53.7)	<0.001
Pre-PCI TIMI 0 or 1, n (%)	812 (58.2)	4399 (56.7)	0.29
Post-PCI TIMI 0 or 1, n (%)	53 (3.8)	180 (2.4)	0.001
Post-PCI TIMI 3, n (%)	1224 (88.6)	7167 (93.7)	<0.001
Drug-eluting stent, n (%)			
Sirolimus	578 (44.4)	3593 (47.9)	0.018
Paclitaxel	494 (37.9)	2540 (33.9)	0.005
Zotarolimus	133 (10.2)	859 (11.5)	0.189
Other stent	98 (7.5)	507 (6.8)	0.317
Total number of stents, n (%)	1.6 ± 0.8	1.5 ± 0.8	0.069
Stent size			
Long (mm)	6.0 ± 0.17	6.3 ± 0.07	0.711
Diameter (mm)	3.1 ± 0.4	3.2 ± 0.4	<0.001
<b>Medical treatment, n (%)</b>			
Unfractionated heparin	863 (58.2)	4869 (58.4)	0.862
Low molecular heparin	541 (36.5)	2979 (35.7)	0.59
Glycoprotein IIb/IIIa Inhibitor	185 (12.4)	1341 (16.0)	<0.001
Aspirin	1469 (98.3)	8334 (99.4)	<0.001
Clopidogrel	1455 (97.4)	8282 (98.8)	<0.001
Cilostazol	515 (34.5)	3292 (39.3)	<0.001
β-Blockers	1057 (70.7)	6638 (79.2)	<0.001
ACE-I	1088 (72.8)	6233 (74.4)	0.214
ARB	294 (19.7)	1479 (17.6)	0.059
Statin	1120 (75.0)	6841 (81.6)	<0.001
Diuretics	481 (32.2)	2595 (31.0)	0.347
Long-acting nitrates	1130 (75.7)	6154 (73.6)	0.077

Data are presented as the n (%) of patients or mean ± SD. PCI, percutaneous coronary intervention; STEMI, ST segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; TIMI, Thrombolysis In Myocardial Infarction; ACC/AHA, American College of Cardiology/American Heart Association; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

### In-hospital events and short-term mortality

There were significant differences in in-hospital death, but not in major bleeding, in the STEMI and NSTEMI groups (Fig. 2).

### One-year outcomes and predictors of major adverse events

Fig. 3A shows the adjusted survival curve for all-cause mortality. Mortality was higher in the octogenarian group. Age (hazard ratio, HR 2.37, 95% confidence interval, CI 1.56–3.63,  $p < 0.001$ ), Killip class ≥ II (HR 2.64, 95% CI 1.73–4.05,  $p < 0.001$ ), STEMI (HR 1.74, 95% CI 1.10–2.75,  $p = 0.018$ ), LVEF < 40% (HR 1.97, 95% CI 1.27–3.05,  $p = 0.002$ ), estimated GFR < 60 ml/min/1.73 m<sup>2</sup> (HR 2.33, 95% CI 1.25–4.32,  $p = 0.008$ ), hs-CRP (HR 1.99, 95% CI 1.25–3.17,  $p = 0.004$ ), and NT-proBNP (HR 2.68, 95% CI 1.49–4.83,  $p = 0.001$ ) were independent predictors for 1-year all-cause mortality according to multivariable Cox proportional hazard analysis (Table 3).

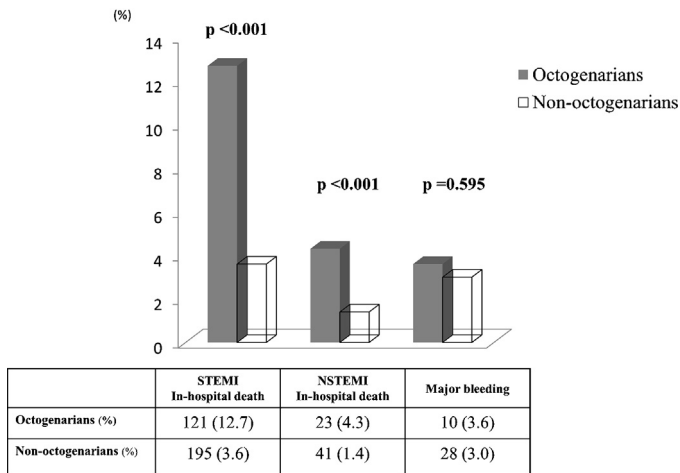
Fig. 3B shows that the composite MACE outcome was more prevalent in octogenarians compared with non-octogenarians. Age (HR 1.53, 95% CI 1.16–2.02,  $p = 0.003$ ), metabolic syndrome (HR 1.29, 95% CI 1.04–1.60,  $p = 0.021$ ), LVEF < 40% (HR 1.88, 95% CI 1.45–2.43,  $p < 0.001$ ), estimated GFR < 60 ml/min/1.73 m<sup>2</sup> (HR 1.83,

95% CI 1.18–2.84,  $p = 0.007$ ), hs-CRP (HR 1.38, 95% CI 1.12–1.72,  $p = 0.003$ ), troponin I (HR 1.27, 95% CI 1.03–1.57,  $p = 0.023$ ), and multivessel disease (HR 1.60, 95% CI 1.29–2.00,  $p < 0.001$ ) were independent predictors for 1-year MACE according to multivariable Cox proportional hazard analysis (Table 3).

Table 4 shows the clinical outcomes in patients who underwent primary PCI with DES. The incidence of 1-year cardiac death and non-cardiac death was significantly higher in octogenarians. There were no significant differences in the rate of 1-year recurrent myocardial infarction (1.3% vs. 0.9%,  $p = 0.68$ ), TLR (2.4% vs. 3.1%,  $p = 0.69$ ), TVR (3.6% vs. 4.3%,  $p = 0.96$ ), or CABG (0.9% vs. 0.9%,  $p = 0.76$ ) between the 2 groups. Subgroup analysis by age demonstrated that an age ≥ 80 years was associated with 1-year all-cause death and 1-year MACE, regardless of the subgroup (Fig. 4). In particular, an age ≥ 80 years in the STEMI subgroup and the estimated GFR < 60 ml/min/1.73 m<sup>2</sup> subgroup was significantly associated with 1-year all-cause mortality.

### Discussion

DES have been reported to dramatically reduce the need for revascularization. However, few reports have described the clinical



**Fig. 2.** Comparison of in-hospital death and major bleeding between octogenarian and non-octogenarian patients. STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction.

impact of DES in octogenarian AMI patients. Devlin et al. reported the management and 6-month outcomes in elderly AMI patients from the Global Registry of Acute Coronary Events (GRACE), but the follow-up period of this study was brief [14]. Takii et al. reported the trends in AMI incidence and mortality from the MIYAGI-AMI Registry Study; however, the data obtained did not accurately reflect the actual conditions prevailing during the DES era [15]. Therefore, the present study can contribute valuable evidence concerning the prognosis of octogenarian AMI patients in the DES era.

The findings reported here revealed the following clinical observations in the KAMIR subgroup analysis. First, the prevalence of concomitant disorders was significantly higher in octogenarian than in non-octogenarian patients. In contrast, octogenarians were

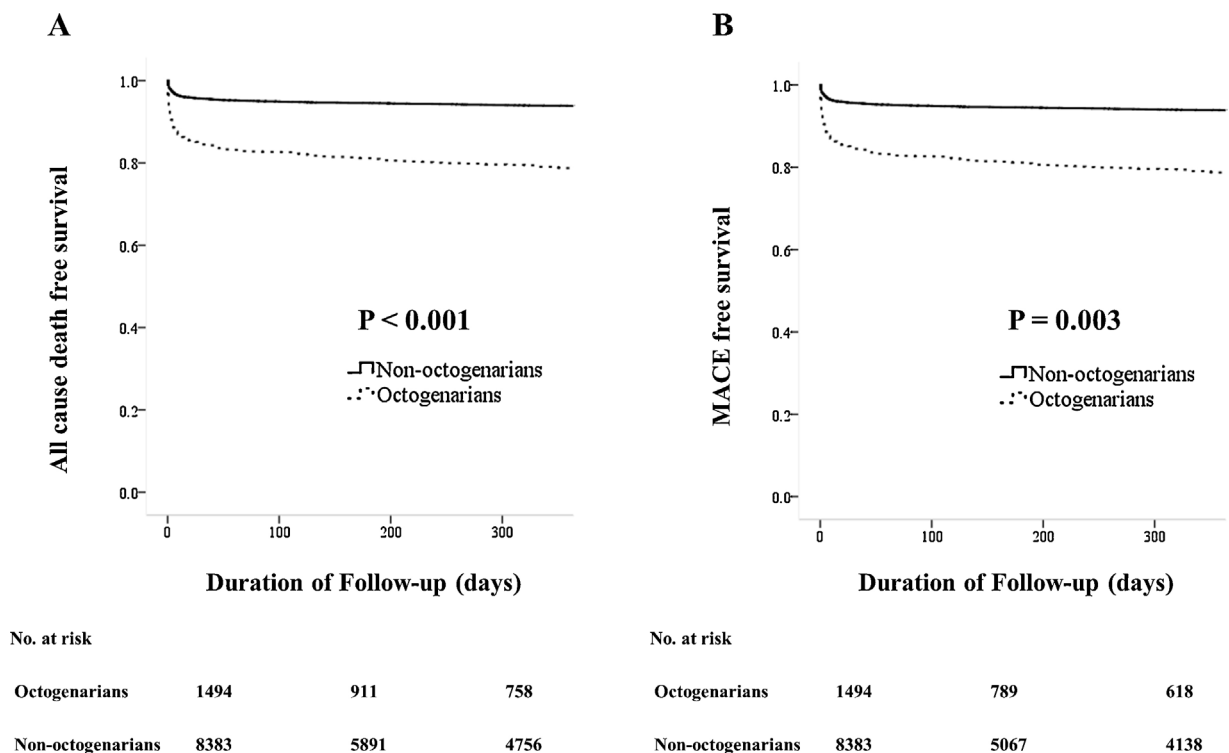
less likely to receive evidenced-based medical treatment, antiplatelet therapy,  $\beta$ -blockers, and statins. Second, even in the DES era, there were significant differences between the 2 groups in the occurrence of all-cause death and MACE at 1-year follow up. However, no significant differences in the rate of 1-year recurrent myocardial infarction, TLR, TVR, recurrent PCI, or CABG were noted between the 2 groups.

The 1-year rates of overall mortality (8.9%) and MACE (18.5%) recorded in the present study were roughly consistent with previous reports. Although octogenarians were more likely to have complex culprit lesions and multivessel disease, TIMI III flow was achieved in 88.5% of cases. Nevertheless, octogenarian AMI patients had higher 1-year mortality and MACE rates compared with non-octogenarians, even in the DES era.

Octogenarian AMI patients, a high-risk population themselves, may often not receive appropriate treatment recommended by current guidelines because of their conditions and comorbidities [16]. Rittger et al. reported that age was the main predictor of a conservative treatment strategy in elderly patients [17]. Medical treatment was also likely to be insufficient for elderly patients. Our study demonstrated that octogenarians were less likely to receive evidence-based medical therapy, which may be a possible reason for the higher incidence of adverse effects or suspected contraindications of medical therapy.

Apart from age, this study identified the following variables to be independent predictors of all-cause death (Killip class  $\geq$  II, STEMI, LVEF  $< 40\%$ , estimated GFR  $< 60$  ml/min/1.73 m<sup>2</sup>, hs-CRP, and NT-proBNP) and MACE (metabolic syndrome, LVEF  $< 40\%$ , estimated GFR  $< 60$  ml/min/1.73 m<sup>2</sup>, hs-CRP, troponin I, and multivessel disease) at 1-year follow up. Post-procedural epicardial flow was not associated with 1-year mortality in this study. The overall high TIMI flow rate (93%) might have affected these results.

It is well known that elderly MI patients have a higher risk of all-cause death and MACE. DES have been reported to dramatically reduce the rate of restenosis and TLR compared with bare-metal



**Fig. 3.** Kaplan–Meier curve with number of patients at risk for octogenarians and non-octogenarians. (A) 1-Year all-cause death-free unadjusted survival curves. (B) Cumulative incidences of 1-year MACE-free unadjusted survival curves. MACE, major adverse cardiac events.



**Table 3**  
Multivariate analysis of all-cause death and MACE at 1-year follow-up.

	All-cause death		MACE	
	p-Value	Hazard ratio (95% CI)	p-Value	Hazard ratio (95% CI)
Age $\geq 80$	<0.001	2.37 (1.56–3.63)	0.003	1.53 (1.16–2.02)
Metabolic syndrome	0.183	1.43 (0.84–2.43)	0.021	1.29 (1.04–1.60)
Killip class $\geq$ II	<0.001	2.64 (1.73–4.05)	0.149	1.20 (0.94–1.55)
STEMI	0.018	1.74 (1.10–2.75)	0.103	1.23 (0.96–1.57)
Multivessel disease	0.475	1.16 (0.77–1.74)	<0.001	1.60 (1.29–2.00)
LVEF < 40%	0.002	1.97 (1.27–3.05)	0.001	1.88 (1.45–2.43)
TnI	0.137	1.37 (0.90–2.11)	0.048	1.27 (1.03–1.57)
Estimated GFR < 60	0.008	2.33 (1.25–4.32)	0.042	1.83 (1.18–2.84)
hs-CRP	0.004	1.99 (1.25–3.17)	0.017	1.38 (1.12–1.72)
NT-proBNP	0.001	2.68 (1.49–4.83)	0.515	1.09 (0.85–1.39)

MACE, major adverse cardiac event; STEMI, ST segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; TnI, troponin I; GFR, glomerular filtration rate; hs-CRP, high-sensitivity C-reactive protein; NT-pro-BNP, N-terminal pro-B type natriuretic peptide; CI, confidence interval.

**Table 4**  
Adjusted cumulative clinical outcomes at 1 year.

	Octogenarians n (%)	Non-octogenarians n (%)	Unadjusted HR (95% CI)	p-Value	Adjusted HR (95% CI)	p-Value
All-cause death	223 (22.3)	359 (6.5)	3.75 (3.17–4.43)	<0.001	2.37 (1.56–3.63)	<0.001
Cardiac death	194 (19.4)	319 (5.8)	3.62 (3.03–4.33)	<0.001	3.03 (2.20–4.17)	<0.001
Non-cardiac death	29 (2.9)	40 (0.7)	4.65 (2.88–7.50)	<0.001	5.68 (2.87–11.2)	<0.001
Recurrent MI	13 (1.3)	52 (0.9)	1.59 (0.86–2.91)	0.14	1.19 (0.52–2.72)	0.68
Recurrent PCI	57 (5.7)	469 (8.5)	0.79 (0.60–1.04)	0.09	0.84 (0.61–1.17)	0.31
TLR	24 (2.4)	170 (3.1)	0.92 (0.60–1.40)	0.69	0.89 (0.52–1.54)	0.69
TVR	36 (3.6)	236 (4.3)	0.99 (0.70–1.41)	0.96	0.99 (0.64–1.54)	0.96
CABG	9 (0.9)	51 (0.9)	1.08 (0.53–2.20)	0.83	0.83 (0.24–2.80)	0.76
MACE	296 (29.6)	909 (16.4)	2.03 (1.78–2.31)	<0.001	1.53 (1.16–2.02)	0.003

Data are presented as the n (%) of patients or mean  $\pm$  SD. HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention; TLR, target lesion revascularization; TVR, target vessel revascularization; CABG, coronary artery bypass grafting; MACE, major adverse cardiac events.

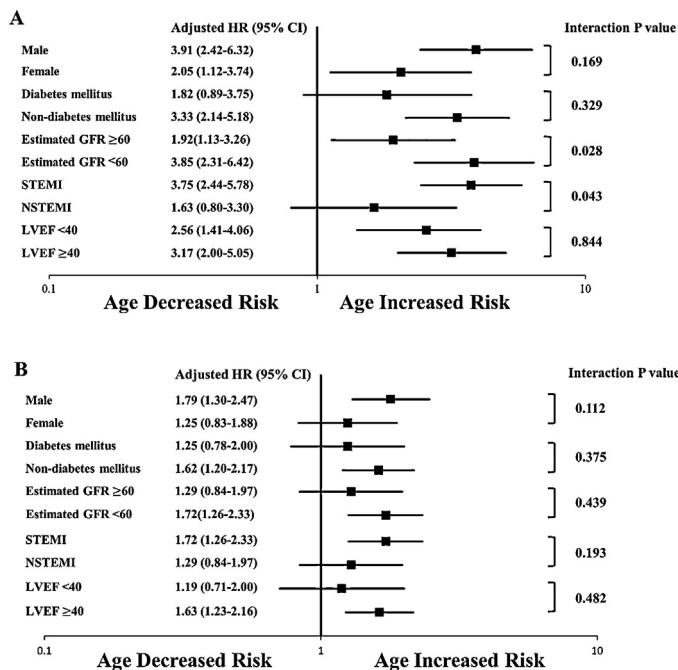
stents (BMSs) [18–20]. In contrast, PCI with DES might be associated with an increase in the rate of stent thrombosis because of the delayed arterial healing response [21,22]. Stent thrombosis is an unusual, but life-threatening complication associated with DES implantation. Spaulding et al. reported that there was no

difference in the rate of stent thrombosis at 1-year follow up among AMI patients; furthermore, the use of DES significantly reduced the rate of TVR [23]. Violini et al. found that the 3-year incidence of MACE, and of TLR and TVR, was lower in the DES (sirolimus-eluting stent) group compared with the BMS group [24]. The present study did not provide follow-up data for stent thrombosis according to the ARC definition.

Elderly patients receiving dual anti-platelet therapy represent a high-risk group for bleeding [25]. However, the data from this registry showed no significant difference in the occurrence of in-hospital major bleeding between the 2 groups. The discrepancy could be attributable to the relatively low use of antiplatelet therapy and the short follow-up period. The present study did not include long-term follow up of major bleeding data. The new-generation DES are reported to reduce the duration of dual anti-platelet therapy without increasing the risk of stent thrombosis [26]. Further study is required to identify long-term major bleeding and optimal anti-platelet therapy for octogenarians.

Subgroup analysis identified that an age  $\geq 80$  years was associated with 1-year all-cause death and MACE regardless of the subgroup. Furthermore, in the subgroups with STEMI or estimated GFR < 60 ml/min/1.73 m<sup>2</sup>, age  $\geq 80$  years was strongly associated with all-cause death. These data were consistent with previous reports from the BMS era. This study was retrospective, but provided a sufficient number of patients to investigate the predictors of all-cause death and MACE at 1 year of follow up. Octogenarians are usually not included in randomized studies; therefore, this study describes the real-world outcomes of octogenarians undergoing PCI in the DES era.

There are few reports regarding octogenarian AMI patients after the use of DES. The results of our study suggested there was no difference in TLR/TVR rates between octogenarians and non-octogenarians. Considering the risks and benefits of PCI for octogenarian AMI patients, PCI with DES might be a comparable therapeutic option.



**Fig. 4.** Estimates of hazard ratios in selected subgroups. Hazard ratios are shown on a logarithmic scale. (A) All-cause death at 1-year follow up. (B) Major adverse cardiac events at 1-year follow up. HR, hazard ratio; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction.

This study had some limitations. First, it was based on registry data, and such studies are always affected by unavoidable selection effects. Significant differences existed in the characteristics of the patients between the 2 groups. However, the KAMIR study involved a prospective design and a large multicenter population base. Therefore, we were able to include most confounders in a multivariable Cox regression model to control the baseline differences to the greatest extent possible. Second, all management decisions were taken by the attending cardiologist. There is a possibility that patients undergoing PCI with DES might have been selected for this study population because of their better condition. Third, routine laboratory tests were performed separately by the different hospitals involved in this study.

In conclusion, octogenarian AMI patients exhibit markedly greater comorbidities and a significantly higher incidence of all-cause death and MACE, even in the DES era. However, KAMIR subgroup analysis revealed no difference in TLR/TVR rates between the 2 groups.

## Acknowledgments

This study was supported by a grant from the Korea Healthcare Technology R&D Project, Ministry for Health, Welfare, and Family Affairs (A084869). This study was performed with the support of the Korean Society of Circulation (KCS) as the memorandum of the 50th Anniversary of the KCS.

## References

- [1] Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13–20.
- [2] Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315–23.
- [3] Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, Colombo A, Schuler G, Barragan P, Guagliumi G, Molnar F, Falotico R. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;346:1773–80.
- [4] Schofer J, Schluter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, Breithardt G. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003;362:1093–9.
- [5] Schampaert E, Cohen EA, Schluter M, Reeves F, Traboulsi M, Tittle LM, Kuntz RE, Popma JJ. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de novo lesions in small native coronary arteries (C-SIRIUS). *J Am Coll Cardiol* 2004;43:1110–5.
- [6] De Gregorio J, Kobayashi Y, Albiero R, Reimers B, Di Mario C, Finci L, Colombo A. Coronary artery stenting in the elderly: short-term outcome and long-term angiographic and clinical follow-up. *J Am Coll Cardiol* 1998;32:577–83.
- [7] DeGeare VS, Stone GW, Grines L, Brodie BR, Cox DA, Garcia E, Wharton TP, Boura JA, O'Neill WW, Grines CL. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention (a pooled analysis of the primary angioplasty in myocardial infarction trials). *Am J Cardiol* 2000;86:30–4.
- [8] Lindsay Jr J, Reddy VM, Pinnow EE, Little T, Pichard AD. Morbidity and mortality rates in elderly patients undergoing percutaneous coronary transluminal angioplasty. *Am Heart J* 1994;128:697–702.
- [9] Santana JO, Haft JJ, LaMarche NS, Goldstein JE. Coronary angioplasty in patients eighty years of age or older. *Am Heart J* 1992;124:13–8.
- [10] Hong YJ, Jeong MH, Abizaid A, Banning A, Bartorelli A, Dzavik V, Ellis SG, Gao R, Holmes Jr DR, Legrand V, Neumann FJ, Spaulding C, Worthley S, Urban P, e-SELECT Registry Investigators. Sirolimus-eluting coronary stents in octogenarians: a 1-year analysis of the worldwide e-SELECT Registry. *JACC Cardiovasc Interv* 2011;4:982–91.
- [11] Kushner FG, Hand M, Smith Jr SC, King 3rd SB, Anderson JL, Antman EM, Bailey SR, Bates ER, Blankenship JC, Casey Jr DE, Green LA, Hochman JS, Jacobs AK, Krumholz HM, Morrison DA, et al. 2009 Focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2009;120:2271–306.
- [12] Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, et al. ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011;32:2999–3054.
- [13] Apple FS, Wu AH, Jaffe AS. European Society of Cardiology and American College of Cardiology guidelines for redefinition of myocardial infarction: how to use existing assays clinically and for clinical trials. *Am Heart J* 2002;144:981–6.
- [14] Devlin G, Gore JM, Elliott J, Wijesinghe N, Eagle KA, Avezum A, Huang W, Brieger D. GRACE Investigators. Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: the Global Registry of Acute Coronary Events. *Eur Heart J* 2008;29:1275–82.
- [15] Takii T, Yasuda S, Takahashi J, Ito K, Shiba N, Shirato K, Shimokawa H. MIYAGI-AMI Study Investigators. Trends in acute myocardial infarction incidence and mortality over 30 years in Japan: report from the MIYAGI-AMI Registry Study. *Circulation* 2010;121:93–100.
- [16] Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliquet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, et al. Guidelines on myocardial revascularization. *Eur Heart J* 2010;31:2501–55.
- [17] Rittger H, Schnupp S, Sinha AM, Breithardt OA, Schmidt M, Zimmermann S, Mahnkopf C, Brachmann J, Rieber J. Predictors of treatment in acute coronary syndromes in the elderly: impact on decision making and clinical outcome after interventional vs. conservative treatment. *Catheter Cardiovasc Interv* 2012;80:735–43.
- [18] Kelbaek H, Helqvist S, Thuesen L, Klovgaard L, Jorgensen E, Saunamaki K, Krusell LR, Botker HE, Engstrom T, Jensen GV. Sirolimus versus bare metal stent implantation in patients with total coronary occlusions: subgroup analysis of the Stenting Coronary Arteries in Non-Stress/Benestent Disease (SCANDSTENT) trial. *Am Heart J* 2006;152:882–6.
- [19] Marroquin OC, Selzer F, Mulukutla SR, Williams DO, Vlachos HA, Wilensky RL, Tanguay JF, Holper EM, Abbott JD, Lee JS, Smith C, Anderson WD, Kelsey SF, Kip KE. A comparison of bare-metal and drug-eluting stents for off-label indications. *N Engl J Med* 2008;358:342–52.
- [20] Stettler C, Wandel S, Allemann S, Kastrati A, Morice MC, Schomig A, Pfisterer ME, Stone GW, Leon MB, de Lezo JS, Goy JJ, Park SJ, Sabaté M, Suttorp MJ, Kelbaek H, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet* 2007;370:937–48.
- [21] Nakazawa G. Stent thrombosis of drug eluting stent: pathological perspective. *J Cardiol* 2011;58:84–91.
- [22] Takayama T, Hiro T, Hirayama A. Stent thrombosis and drug-eluting stents. *J Cardiol* 2011;58:92–8.
- [23] Spaulding C, Henry P, Teiger E, Beatt K, Bramucci E, Carrie D, Slama MS, Merkely B, Erglis A, Margheri M, Varenne O, Cebrian A, Stoll HP, Sneed DB, Bode C. Sirolimus-eluting versus uncoated stents in acute myocardial infarction. *N Engl J Med* 2006;355:1093–104.
- [24] Violini R, Musto C, De Felice F, Nazzaro MS, Cifarelli A, Petitti T, Fiorilli R. Maintenance of long-term clinical benefit with sirolimus-eluting stents in patients with ST-segment elevation myocardial infarction 3-year results of the SESAMI (sirolimus-eluting stent versus bare-metal stent in acute myocardial infarction) trial. *J Am Coll Cardiol* 2010;55:810–4.
- [25] Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, Cacoub P, Cohen EA, Creager MA, Easton JD, Flather MD, Haffner SM, Hamm CW, Hankey GJ, Johnston SC, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med* 2006;354:1706–17.
- [26] Damman P, Iniguez A, Klomp M, Beijk M, Woudstra P, Silber S, Ribeiro EE, Suryapranata H, Sim KH, Tijssen JG, de Winter RJ. e-HEALING investigators. Coronary stenting with the Genous Bio-Engineered R Stent in elderly patients. *Circ J* 2011;75:2590–7.